IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BRISTOL-MYERS SQUIBB CO. and E. R. SQUIBB & SONS L.L.C.,	)	
Plaintiffs,	)	
vs.	)	**Case No. 22-346-MFK**
ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA UK LTD.,	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER
REGARDING CLAIM CONSTRUCTION

MATTHEW F. KENNELLY, District Judge:

Bristol-Myers Squibb Co. and E. R. Squibb & Sons, L.L.C. (collectively, BMS) have sued AstraZeneca Pharmaceuticals LP and AstraZeneca UK Ltd. (collectively, AstraZeneca) for infringement of BMS's patents related to an immunotherapy treatment of late-stage non-small cell lung cancer (NSCLC). The parties seek construction of eight claim terms from the asserted patents. The parties submitted written briefs, and the Court held a claim construction hearing on April 7, 2023. This opinion sets forth the Court's construction of the disputed claim terms.

Background

In 2014, BMS's drug nivolumab (sold commercially as Opdivo) was approved by the FDA for treatment of melanoma. Opdivo was subsequently approved for the treatment of other cancers, including NSCLC. In 2018, AstraZeneca's drug durvalumab (sold commercially as Imfinzi) was approved by the FDA to treat patients with stage III

NSCLC. Imfinzi is also sold to treat other cancers. BMS accuses AstraZeneca's competing drug of infringing its asserted patents. Specifically, BMS asserts eight patents in this case: U.S. Patent Nos. 9,580,505 (the '505 Patent); 9,580,507 (the '507 Patent); 10,138,299 (the '299 Patent); 10,266,594 (the '594 Patent); 10,266,595 (the '595 Patent); 10,266,596 (the '596 Patent); 10,308,714 (the '714 Patent); and 10,323,092 (the '092 Patent).

These patents relate to an immunotherapy cancer treatment. T cells can fight cancer by destroying cancer cells, but T cell activity can be decelerated when an inhibitory protein on the T cell, called PD-1, binds to a protein named PD-L1. For healthy individuals, this process prevents the immune system from damaging normal cells. In cancer patients, however, a tumor cell with PD-L1 on its surface can bind to PD-1 to inhibit the T cell from killing the cancer cells. To disrupt this, an anti-PD-L1 antibody can bind to PD-L1 on the cancer cell to prevent it from inhibiting T cell activity.

Two of BMS's asserted patents, the '505 and '507 patents (which the parties collectively call "the Korman patents"), relate to anti-PD-L1 antibodies. Specifically, the patents cover "isolated monoclonal antibodies . . . that bind to PD-L1." '505 Patent at 1:63–65. Because both patents "ha[ve] the same specification," the parties only cite to the specification of the '505 patent. Joint Cl. Const. Chart at 6 n.1. Claim 1 of the '505 patent is directed to "[a]n anti-PD-LI monoclonal antibody, or an antigen-binding portion thereof, which cross-competes for binding to human PD-L1 with a reference antibody, wherein the reference antibody comprises" several specific heavy and light chain variable regions. '505 Patent at 139:55–141:21.

BMS's remaining asserted patents are referred collectively by the parties as "the

Cogswell patents" and claim priority to applications filed in 2012 and 2013. The Cogswell patents relate to a method of treating cancer by administering an anti-PD-L1 antibody to a patient. Each Cogswell patent "ha[s] the same specification," Joint Cl. Const. Chart at 10 n.2, but the claims are directed to treating different cancers. Most of the disputed claim terms come from the '092 patent, which claims "[a] method of treating a late stage non-small cell lung cancer (NSCLC) tumor." '092 Patent at 101:49–50.

The Court addresses the disputed claim terms in the order discussed by the parties at the claim construction hearing. Because each disputed phrase has multiple proposed constructions, the Court will not list each one here, but instead will do so at the beginning of the section of the analysis discussing each phrase. The parties' proposed constructions are taken from the joint claim construction chart.

Discussion

The meaning of patent claims is a question of law for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 387–88 (1996). During claim construction, a court construes the words of a claim in accordance with their "ordinary and customary meaning," namely "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc). When the meaning of a term is "not immediately apparent," a court looks to "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence" to determine "what a person of skill in the art would have understood disputed claim language to mean." *Id.* at 1314 (internal quotation marks omitted). A court "begin[s] by considering the

language of the claims themselves," but claims must also "be read in view of the specification, of which they are a part." *Grace Instrument Indus., LLC v. Chandler Instruments Co.*, 57 F.4th 1001, 1008 (Fed. Cir. 2023) (internal quotation marks omitted). The specification "is the single best guide to the meaning of a disputed term" and "[u]sually . . . is dispositive." *Phillips*, 415 F.3d at 1315 (internal quotation marks omitted).

A. Korman patents

1. "Cross-competes for binding to human PD-L1 with a reference antibody"

Claim Terms	Plaintiffs' Proposal	Defendants' Proposal
"cross-competes for binding to human PD-L1 with a reference antibody" ('505 Patent, claims 1, 29; '507 Patent, claim 1)	"Inhibits the binding of a reference antibody to human PD-L1 by, for example, Biacore analysis, ELISA analysis, or flow cytometry."	"binds to the same epitope on PD-L1"

Claims 1 and 29 from the '505 patent and claim 1 of the '507 patent cover "[a]n anti-PD-L1 monoclonal antibody, or antigen-binding portion thereof, which cross-competes for binding to human PD-L1 with a reference antibody." *See, e.g.*, '505 Patent at 139:55–141:21. The parties dispute the meaning of "cross-competes for binding to human PD-L1." *Id.* BMS contends that "cross-competition is demonstrated by inhibition of binding" tested in "binding experiments," such as "BIAcore analysis, ELISA analysis, or flow cytometry." Pls.' Opening Mem. at 6–7. AstraZeneca contends that "an antibody 'cross-competes for binding to human PD-L1' with a reference antibody if it 'binds to the same epitope on PD-L1' as the reference antibody." Defs.' Resp. Br. at 24.

AstraZeneca primarily argues that the specification expressly defines the claim

term in accordance with its proposed construction. In describing an embodiment of the patented invention, the specification explains that "the invention provides antibodies that bind to the same epitope on human PD-L1 as any of the PD-L1 monoclonal antibodies of the invention (i.e., antibodies that have the ability to cross-compete for binding to PD-L1 with any of the monoclonal antibodies of the invention)." '505 Patent at 27:27–32. AstraZeneca contends that "i.e." signals the patentee's intent to define the term "cross-competes." Defs.' Resp. Br. at 24 (citing *TF3 Ltd. v. Tre Milano, LLC*, 894 F.3d 1366, 1372 (Fed. Cir. 2018) ("The usage 'i.e.' ('id est' or 'that is'), signals an intent to define the word to which it refers." (internal quotation marks omitted))).

AstraZeneca's contention is unpersuasive for two reasons. First, the sentence AstraZeneca emphasizes is defining "antibodies that bind to the same epitope" as "antibodies that have the ability to cross-compete for binding," not the other way around. '505 Patent at 27:27–32. The "natural interpretation of '*i.e.*'" is to read "the word that precedes '*i.e.*'[] to be defined by . . . the term that follows '*i.e.*'" *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1201 (Fed. Cir. 2013) ("[W]e are not proposing that the definition of 'two-dimensions' (the term that follows '*i.e.*' here) be restricted to or defined as only 'beads' (the word that precedes '*i.e.*')."); *see also Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1370 (Fed. Cir. 2012) (declining to interpret "each side of the disk—i.e., each recording plane" as "equat[ing] a 'recording plane' to 'a side of the disk'").

Second, the relationship between cross-competition and the epitope is explained by the rest of the paragraph. After the opening sentence AstraZeneca cites, the paragraph lists "the reference antibod[ies] for cross-competition studies." '505 Patent at

27:32–33. It proceeds to explain:

> Such cross-competing antibodies can be identified based on their ability to cross-compete with [the reference antibodies] in standard PD-L1 binding assays. For example, BIAcore analysis, ELISA assays, or flow cytometry may be used to demonstrate cross-competition with the antibodies of the current invention. The ability of a test antibody to inhibit the binding of, for example, [the reference antibodies], to human PD-L1 demonstrates that the test antibody can compete with [the reference antibodies] for binding to human PD-L1 and thus binds to the same epitope on human PD-L1 as [the reference antibodies].

'505 Patent at 27:55–28:1. This paragraph, when read as a whole, explains that to determine if a test antibody cross-competes with a reference antibody, standard PD-L1 binding assays, such as BIAcore analysis, ELISA assays, or flow cytometry, are used to test if the antibody inhibits the binding of a reference antibody. If a test antibody inhibits the binding of a reference antibody, it can be inferred that the antibodies bind to the same epitope. But the patent never suggests that one could work backwards. In other words, the patent does not teach to look at whether two antibodies bind to the same epitope to determine that those antibodies cross-compete. Rather, an example described later in the patent specification explains that "[b]inding specificity[] and cross-competition were examined by flow cytometry." *Id.* at 68:50–53.

Thus, the Court construes "cross-competes for binding to human PD-L1 with a reference antibody" to mean inhibits the binding of a reference antibody to human PD-L1 in standard PD-L1 binding assays. The specification explains that BIAcore analysis, ELISA assays, and flow cytometry are examples of standard PD-L1 binding assays, but BMS agreed at the claim construction hearing that it is unnecessary to list these examples in the Court's construction.

In addition to aligning with the specification, the Court's construction is also

supported by the prosecution history. During prosecution, the applicant submitted the results of flow cytometric analyses, concluding that because several antibodies were "significantly blocked by each of the tested anti-PD-L1 [antibodies]," the "data show[ed] that [these antibodies] cross-compete with all of the [antibodies] tested . . . for binding to the same epitope region of human PD-L1." Pls.' Opening Mem. at 9 (emphasis omitted) (quoting J.A. Part 8 at 2411). This evidence is consistent with the Court's conclusion that experimental test results for inhibited binding determines whether two antibodies cross-compete.

AstraZeneca contends that this experiment data shows that it is unclear how much an antibody must be blocked for it to "cross-compete." AstraZeneca argues that because BMS's proposed construction does not clarify how the standard PD-L1 binding assays should be conducted or what results must be obtained, it "provides no reasonable certainty to the person of skill in the art regarding the scope of the claim, and, if adopted, would render the claims invalid." Defs.' Resp. Br. at 27. "However, a sound claim construction need not always purge every shred of ambiguity." *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 806 (Fed. Cir. 2007). And, in any event, "[w]here the meaning of a claim term is clear, as it is here, [courts] do not rewrite the claim to preserve its validity." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1374 (Fed. Cir. 2014). The Court declines to use AstraZeneca's validity-based argument as a means of claim construction. *See id.* ("Courts should be cautious not to allow claim construction to morph into a mini-trial on validity."); *Bennett Regul. Guards, Inc. v. Atlanta Gas Light Co.*, 825 F. App'x 773, 777 (Fed. Cir. 2020) ("[C]laim terms should be given their plain and ordinary meaning to one of skill in the art at the relevant time and

cannot be rewritten by the courts to save their validity.") (internal quotation marks omitted).

At the claim construction hearing, AstraZeneca raised a related issue, specifically, that BMS's proposed construction does not explain which experiments can be used to show inhibited binding. But "[b]ecause the claim language does not require a particular form of testing, this inquiry is not a claim construction question." *Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co.*, 425 F.3d 1366, 1377 (Fed. Cir. 2005), *overruled on other grounds by Cardiac Pacemakers, Inc. v. St. Jude Med., Inc.*, 576 F.3d 1348 (Fed. Cir. 2009); *see also Lazare Kaplan Int'l, Inc. v. Photoscribe Techs., Inc.*, 628 F.3d 1359, 1376 (Fed. Cir. 2010) ("[T]he parties' dispute concerns factual questions relating to the test for infringement and not the legal inquiry of the appropriate scope of the 'positional accuracy' limitation."). AstraZeneca's contention is therefore inappropriate to resolve as a part of claim construction. *See ADC Telecomms., Inc. v. Switchcraft, Inc.*, 281 F. App'x 989, 992 (Fed. Cir. 2008) ("The parties' dispute over the proper testing method is therefore a factual question that the district court properly submitted to the jury.").

2. "Reference antibody"

Claim Terms	Plaintiff's Proposal	Defendant's Proposal
"reference antibody" ('505 Patent, claims 1, 29; '507 Patent, claim 1)	"An antibody used as a reference in a cross-competition experiment"	"Antibody" is defined to include whole antibodies and any antigen binding fragment or single chain thereof. If a constant region is present, it can be any constant region, e.g., IgG, IgM, etc. "Antigen binding fragment" also is defined and

		includes, inter alia, an Fab fragment and an scFv."

Both parties agree that the patents' specification expressly defines "antibody." *See* Patent '505 at 14:57–14:59 ("The term 'antibody' as referred to herein includes whole antibodies and any antigen binding fragment (i.e., 'antigen-binding portion') or single chains thereof."). The dispute is whether that definition "applies equally to 'reference antibody.'" Defs.' Resp. Br. at 29. AstraZeneca contends that it does without citing to any supporting intrinsic or extrinsic evidence.

The Court declines to read "reference" out of the claim as AstraZeneca proposes. "An interpretation that renders language superfluous is strongly disfavored." *VirnetX Inc. v. Apple Inc.*, 792 F. App'x 796, 811 (Fed. Cir. 2019); *see also Becton, Dickinson & Co. v. Tyco Healthcare Grp.*, 616 F.3d 1249, 1257 (Fed. Cir. 2010) ("Claims must be interpreted with an eye toward giving effect to all terms in the claim.") (internal quotation marks omitted). The claim language already sufficiently defines "a reference antibody" as an antibody that "cross-competes for binding to human PD-L1" with the claimed "anti-PD-L1 monoclonal antibody." '505 Patent at 139:55–58. The claim language further explains that "the reference antibody comprises" several specific heavy and light chain variable regions. *Id.* at 139:58–141:18. Moreover, the specification clearly describes that a "reference antibody" is used "for cross-competition studies." *Id.* at 27:32–33. Therefore, to the extent "reference antibody" requires construction, the Court construes the term in accordance with its ordinary and customary meaning—namely, an antibody used as a reference in a cross-competition experiment.

B. Cogswell patents

1. Tumor characterization terms

a. "Late stage" and "advanced"

Claim Terms	Plaintiff's Proposal	Defendant's Proposal
"late stage non-small cell lung cancer (NSCLC) tumor" ('092 Patent, claim 1)	"Stage III or stage IV non-small cell lung cancer (NSCLC) tumor."	"Stage IV/metastatic non-small cell lung cancer (NSCLC) tumor"
"the tumor is advanced or recurrent" ('092 Patent, claim 3)	"Advanced" should be construed according to its plain and ordinary meaning, which is: "cannot be surgically removed in its entirety." No construction is needed for the remainder of the term.	"advanced" has the same meaning as "late stage" ("stage IV/metastatic")

AstraZeneca proposes that the terms "late stage" and "advanced" from claims 1 and 3, respectively, of the '092 patent both mean "stage IV/metastatic" NSCLC. Defs.' Resp. Br. at 5. BMS contends that the terms have separate meanings. BMS proposes that "late stage" means stage III or IV NSCLC and that "advanced" means "cannot be surgically removed in its entirety." Pls.' Opening Mem. at 12–14.

The threshold issue is whether "late stage" and "advanced" are synonymous. Both parties agree that the examiner used the terms synonymously during the '092 patent's prosecution history. Claim 1, when originally submitted to the PTO as claim 18 of the applicant's second preliminary amendment, claimed:

> A method of treating a late stage non-small cell lung cancer (NSCLC) tumor in a human subject, comprising administering to the subject about 10 mg/kg of an anti-PD-L1 antibody every 2 weeks, wherein the anti-PD-L1 antibody is administered intravenously over 60 minutes infusion; and wherein the subject is pretreated for a chemotherapy and a radiotherapy.

J.A. Part 7 at 1795. The examiner rejected the claim as obvious and therefore "unpatentable over Korman et al. (US 2009/0055944)." *Id.* at 1805. In rejecting the claim, the examiner explained that "a method of treating a late-stage NSCLC is inherent" in the prior patent's teachings. *Id.* at 1806. As support, the examiner quoted the '092 patent's specification submitted to the PTO, which stated that "[t]he majority of [NSCLC] subjects (approximately 78%) are diagnosed with advanced/recurrent or metastatic disease." *Id.* (alterations in original). Critically, the examiner stated that "[i]n this context, the terms 'late-stage' and 'advanced' cancer are interpreted as being synonymous." *Id.* In response, the applicant amended the claim to add the additional limitation that "at least 1% of tumor cells in the tumor exhibit membrane PD-L1 expression." *Id.* at 1839. The claim was then approved by the examiner. In the "Reasons for Allowance," the examiner reiterated that advanced means late stage. *See id.* at 1853 (comparing the '092 patent to "the claims of the '082 Patent," which "recite a method of treating an NSCLC tumor (claim 4), wherein . . . the cancer is advanced [i.e. late stage]") (alteration in original).

"Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Phillips*, 415 F.3d at 1317. "[I]n ascertaining the scope of an issued patent, the public is entitled to equate an inventor's acquiescence to the examiner's narrow view of patentable subject matter with abandonment of the rest." *TorPharm, Inc. v. Ranbaxy Pharms., Inc.*, 336 F.3d 1322, 1330 (Fed. Cir. 2003). "Such acquiescence may be found where the patentee narrows his or her claims by amendment or lets stand an examiner's restrictive interpretation of a claim." *Id.* (citations omitted). "[T]o avoid any chance for disclaimer," an applicant "can

challenge an examiner's characterization" of claim terms. *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1096 (Fed. Cir. 2013). An applicant's "failure to challenge the Examiner's understanding amounts to a disclaimer." *SandBox Logistics LLC v. Proppant Express Invs. LLC*, 813 F. App'x 548, 554 (Fed. Cir. 2020).

In this case, BMS amended its claim in response to the examiner's interpretation of late stage as synonymous with advanced and never challenged the examiner's consistent characterization of the terms. This constitutes a disclaimer of any meaningful difference between "late stage" and "advanced." Indeed, BMS continues to rely in its briefs on the examiner's understanding of "late stage" as synonymous with "advanced" to argue that "late stage" includes stage III tumors because "advanced" includes stage III tumors.

In addition, BMS's support for its proposed construction of advanced is unpersuasive. The plain and ordinary meaning of "advanced" is not "cannot be surgically removed in its entirety" as BMS contends, Pls.' Opening Mem. at 14, and BMS does not provide any source that defines "advanced" as it proposes. To support its construction, BMS refers to a study that was cited in the specification related to "advanced NSCLC." '092 Patent at 55:33–37 ("Pemetrexed has also been shown to produce clinically equivalent efficacy outcomes but with significantly fewer side effects compared with docetaxel in the 2 L treatment of patients with advanced NSCLC (Hanna et al., 2004)."). Patients were eligible for the Hanna et al. study on advanced NSCLC if they had "confirmation of NSCLC with stage III or IV disease not amenable to curative therapy." Pls.' Opening Mem. Ex. H at 1590. Although this supports that "advanced" encompasses both stage III and IV cancers, BMS does not provide any evidence that

"not amenable to curative therapy" means "cannot be surgically removed in its entirety."

BMS next points to the specification's statement that "for patients with Stage I or II disease, surgery provides the best chance for cure." Pls.' Opening Mem. at 14 (quoting '092 Patent at 55:3–5). This sentence does not even use the term "advanced." The fact that surgery may be the best curative treatment at stage I or II does not, without more, imply that "advanced" means "cannot be surgically removed in its entirety." Thus, neither source defines "advanced" as BMS proposes.

Lastly, BMS contends that construing "advanced" and "late stage" to have the same meaning would make certain dependent claims redundant. *Compare* '092 Patent at 101:49–50 ("A method of treating a late stage non-small cell lung cancer (NSCLC) tumor . . . ."); *with id.* at 101:58–59 ("The method of claim 1, wherein the tumor is advanced or recurrent."). Although the doctrine of claim differentiation "creates a presumption that each claim in a patent has a different scope[,] it is not a hard and fast rule of construction." *Seachange Int'l, Inc. v. C-COR, Inc.*, 413 F.3d 1361, 1369 (Fed. Cir. 2005) (internal quotation marks omitted). "[A]ny presumption created by the doctrine of claim differentiation will be overcome by a contrary construction dictated by the written description or prosecution history." *Littelfuse, Inc. v. Mersen USA EP Corp.*, 29 F.4th 1376, 1380 (Fed. Cir. 2022) (internal quotation marks omitted); *see also Seachange*, 413 F.3d at 1369 ("Claims that are written in different words may ultimately cover substantially the same subject matter.") (alterations accepted) (internal quotation marks omitted). Because the prosecution history dictates that "late stage" and "advanced" are synonymous, BMS's claim differentiation argument is unavailing. *See Biogen*, 713 F.3d at 1097 ("Our cases make clear . . . that where found, prosecution

history disclaimer can overcome the presumption of claim differentiation.").

Having concluded that "advanced" and "late stage" are synonyms, the question remains whether the terms mean stage III and IV cancer, as BMS contends, or only stage IV, as AstraZeneca contends. On this point, the Court agrees with BMS and construes both terms to mean stage III or IV.

Although the specification does not expressly define "late stage" or "advanced," it indicates that the terms encompass both stage III and IV cancers. First, the specification references two studies on advanced disease that included both stage III and IV patients. *See* '092 Patent at 1:61–66, 55:33–37. Second, in discussing the "tumor regression and disease stabilization induced by nivolumab in heavily-pretreated patients with advanced NSCLC" and other cancers, the specification cites to four clinical trials that were performed on patients with stage III or IV cancer. '092 Patent at 31:6–65. By consistently using the term "advanced" to refer to stage III and IV patients, the specification supports the Court's construction.[1]

In contending that "advanced" only includes stage IV, AstraZeneca primarily relies on the specification's reference to the 2013 NCCN Guidelines. *See* '092 Patent at 53:19–27 ("[T]he National Comprehensive Cancer Network (NCCN), an alliance of 21 major cancer centers in the USA, publishes the NCCN Clinical Practice Guidelines in Oncology . . . that provide detailed up-to-date information on the standard-of-care

[1] BMS also points to an AstraZeneca patent filed in 2021 that defines late stage to include stage III or IV and a 2020 study that grouped stages III and IV together as late stage. "[A] court must construe the claim language according to the standard of what those words would have meant to one skilled in the art as of the application date." *Wiener v. NEC Elecs., Inc.*, 102 F.3d 534, 539 (Fed. Cir. 1996). BMS has not sufficiently explained how this extrinsic evidence that post-dates the '092 patent is relevant, so the Court declines to consider it.

treatments for a wide variety of cancers (see NCCN GUIDELINES®, 2013).").
AstraZeneca emphasizes the 2013 NCCN Guidelines' statement that "locally advanced disease is now stage III; advanced disease is now stage IV." Defs.' Resp. Br. at 8 (emphasis omitted) (quoting Ex. 7 at MS-7).

But the 2013 NCCN Guidelines also make several references to advanced NSCLC as including stages III and IV. *See* Defs.' Resp. Br. Ex. 7 at MS-22 ("An analysis of 5 clinical trials in mainly Western patients (n = 223) with advanced NSCLC (stage IIIB or IV) . . . ."), MS-35 ("A noninferiority trial in 1725 patients with advanced NSCLC (either stage IIIB or IV; most were stage IV) . . . ."). Thus, contrary to AstraZeneca's assertion, the 2013 NCCN Guidelines do not strictly define "advanced" as stage IV and "locally advanced" as stage III. Rather, the 2013 NCCN Guidelines indicate that these terms can overlap. Indeed, the specification suggests that late stage and advanced cancer can include locally advanced cancer. It states that "[r]ecent successes include . . . crizotinib (XALKORI®) to treat the 5% of patients with late-stage non-small cell lung cancers" who express a certain gene. '092 Patent at 2:26–33. The 2013 NCCN Guidelines explain that "[c]rizotinib . . . is approved by the FDA for patients with locally advanced or metastatic NSCLC." Defs.' Resp. Br. Ex 7 at MS-10.

AstraZeneca's reference to dependent claims 2 and 3 of the '299 patent does not compel a different result. AstraZeneca contends that these claims, which recite "advanced" and "locally advanced," respectively, illustrate that "BMS knew how to claim stage III cancer when it wanted to." Defs.' Resp. Br. at 9 (quoting '299 Patent at 101:62–64). But this assumes that "locally advanced" means stage III. The specification belies this assumption, clearly stating instead that "locally advanced"

includes stage II. *See* '092 Patent at 54:11–13 ("Partial nephrectomy is generally not suitable for patients with locally advanced tumors (Stage II and III) . . . ."). Therefore, the specification, read as a whole, indicates that late stage and advanced NSCLC tumors refer to both stages III and IV NSCLC, which includes stage III locally advanced NSCLC tumors.

Lastly, AstraZeneca contends that "late stage" means only stage IV because the specification states that the "median O[verall] S[urvival] for late stage patients is just 1 year." Defs.' Resp. Br. at 9 (quoting '092 Patent at 54:59–60). AstraZeneca argues that this demonstrates that "late stage" refers to stage IV because only stage IV patients have a one-year survival rate. *See* Defs.' Resp. Br. Ex. 8. But the specification does not cite its source for this statistic, and different sources point in different directions. For example, BMS cites another study showing that the overall survival rate for stage III *and* IV patients was 12 months. Pls.' Reply Br. Ex. T at 310. BMS contends that the study it cites is the more likely source of the specification's statistic because AstraZeneca's cited study post-dates the patent. Thus, rather than dictate a contrary construction, this statistic from the specification is entirely consistent with the Court's construction.[2]

b. "Metastatic"

Claim Terms	Plaintiff's Proposal	Defendant's Proposal
"the tumor is metastatic"	Metastatic means "cancer cells have left the primary tumor and spread from	Metastatic means "the tumor has formed a secondary tumor in a

[2] In a footnote, AstraZeneca also argues that the specification's statement that the "5-year survival rate for late-stage MEL is currently only 15%," '092 Patent at 54:6–7, shows that "late stage" means stage IV because another study references a *four*-year survival rate for stage IV melanoma patients of "~15%." Defs.' Resp. Br. at 9 n.6 (quoting Ex. 9 at 2174). The specification again does not cite its source for this statistic. Given the uncertainty with these statistics discussed above and the clear mismatch between this source and the specification, this extrinsic evidence is similarly unavailing.

('299 Patent, claim 4; '594 Patent, claim 4; '595 Patent, claim 4; '596 Patent, claim 4; '714 Patent, claim 4; '092 Patent, claim 4) "the tumor is locally advanced or metastatic" ('594 Patent, claim 29; '595 Patent, claim 29; '596 Patent, claim 29)	where the tumor first formed."	distant part of the body"

The parties dispute how far cancer cells must spread for the tumor to be "metastatic" as the claim uses that term. BMS contends that any spread from the location of the first tumor is sufficient. AstraZeneca contends that "[r]egional or localized movement of the cancer is separate and distinct from metastatic disease where the cancer has spread to distant locations." Defs.' Resp. Br. at 12. The Court agrees with BMS that distant spread is not required and construes "metastatic" to mean that cancer cells have left the primary tumor and spread from where the tumor first formed.

The Court's construction is most consistent with the specification.[3] The specification states that "clinical responses . . . were observed . . . in various sites of metastasis including liver, lung, lymph nodes, and bone." '092 Patent at 30:10–17. Although AstraZeneca emphasizes the inclusion of liver and bone in this sentence, it does not dispute that lymph nodes are not distant sites. The specification further

[3] Although this term appears in multiple patent claims, the joint claim construction chart notes that these patents share the same specification. *See* Joint Cl. Const. Chart at 10 n.2. Both parties only cite to the '092 patent specification, so the Court follows suit.

explains that "[u]nregulated cell division and growth . . . results in the formation of malignant tumors that invade neighboring tissues and may also metastasize to distant parts of the body through the lymphatic system or bloodstream." *Id.* at 9:42–48. If "metastatic" required distant spread, then the phrase "to distant parts of the body" in this sentence would be redundant. AstraZeneca argues that this sentence draws a distinction "between merely invading local tissue and metastasizing to distant body parts." Defs.' Resp. Br. at 12. But that does not explain why the specification includes "to distant parts of the body," because if AstraZeneca's proposal were correct, the sentence could have established the same distinction by simply stating "invade neighboring tissues and may also metastasize."

Moreover, the extrinsic evidence AstraZeneca relies on does not support its proposed construction. First, AstraZeneca cites the Merriam-Webster Dictionary's definition of "metastasis," which is "the spread of a disease-producing agency (such as cancer cells) from the initial or primary site of disease to another part of the body." *Id.* (quoting Ex. 11). This definition does not require distant spread and therefore supports the Court's construction, not AstraZeneca's. Second, AstraZeneca again cites to the 2013 NCCN Guidelines, asserting that it distinguishes between cases where "the cancer had spread to regional lymph nodes or directly beyond the primary site" from cases where "the cancer had already metastasized (distant stage)." Defs.' Resp. Br. Ex. 7 at MS-7. But elsewhere the 2013 NCCN Guidelines use "metastasis" to refer both to "regional lymph node metastasis" and "distant metastasis." *Id.* at ST-1. Finally, AstraZeneca cites to the 2022 NCCN Guidelines for Patients, contending that "metastatic lung cancer" is cancer that "appears in distant body parts." Defs.' Resp. Br.

at 12 (citing Ex. 4 at 9). Even assuming the 2022 NCCN Guidelines are relevant to the meaning of "metastatic" at the time the Cogswell patents were filed, the glossary expressly defines "metastasis" as "[t]he spread of cancer from the first tumor to a new site," which also supports the Court's construction. Defs.' Resp. Br. Ex. 4 at 66.

2. "Pretreated"

Claim Terms	Plaintiff's Proposal	Defendant's Proposal
"wherein the subject is pretreated for a chemotherapy and a radiotherapy" ('092 Patent, claim 1)	"The subject previously received a chemotherapy and a radiotherapy treatment."	"pretreated" means "wherein the subject has failed on a chemotherapy and a radiotherapy"

The parties dispute whether "pretreated" requires the subject to have "failed" on the prior treatment. BMS contends that "pretreated for a chemotherapy and a radiotherapy" only requires the subject to have "previously received a chemotherapy and a radiotherapy treatment." Pls.' Opening Mem. at 16. AstraZeneca contends that "pretreated" contains the additional requirement that the patient "failed on a chemotherapy and a radiotherapy," or, in other words, "the cancer must have progressed (i.e., the tumor grew and the cancer got worse) after receiving these treatments." Defs.' Resp. Br. at 15–16. The Court rejects AstraZeneca's interpretation and construes "wherein the subject is pretreated for a chemotherapy and a radiotherapy" to mean that the subject previously received a chemotherapy and a radiotherapy treatment.

The ordinary and customary meaning of "pretreat" is that the patient was previously treated, not necessarily that those treatments failed. Indeed, the specification describes this exact meaning. *See* '092 Patent at 32:29–33 ("In certain

embodiments of any of the therapeutic methods disclosed herein, the subject has been pre-treated for the cancer; for example, the subject had undergone at least one, two, or three prior lines of therapy for cancer.").

AstraZeneca contends that the specification "emphasizes its goal in providing care to 'treatment-refractory metastatic NSCLC' patients." Defs.' Resp. Br. at 18 (quoting '092 Patent at 39:25–27). Even assuming this language from the specification means, as AstraZeneca contends, "patients for whom prior treatment has been unsuccessful," *id.*, this sentence from the specification does not emphasize such patients as a goal, let alone define "pretreated." *See* '092 Patent at 39:23–27 ("[I]mmunotherapy . . . is not applicable only to 'immunogenic' tumor types . . ., but is also effective with a broad range of cancers, including treatment-refractory metastatic NSCLC . . . .").

"A patentee is normally entitled to the full scope of its claim language, and a departure from this general rule may be warranted only where the patentee either clearly sets forth a different definition of a claim term in the specification or disavows the full scope of the claim term during prosecution." *Duncan Parking Techs., Inc. v. IPS Grp., Inc.*, 914 F.3d 1347, 1364 (Fed. Cir. 2019) (citation omitted). In contending that "pretreated" requires failure on prior therapies, AstraZeneca points to Example 11 in the specification. AstraZeneca asserts that Example 11 is the only clinical trial using a PD-L1 antibody, and it required patients to "have failed at least one prior tumor-appropriate therapy." Defs.' Resp. Br. at 17 (quoting '092 Patent at 67:38–41). One example where a clinical trial required patients to have failed a prior therapy is not sufficient to narrow the meaning of this unambiguous claim term. *See Unwired Planet, LLC v. Apple Inc.*,

829 F.3d 1353, 1359 (Fed. Cir. 2016) ("[W]e have repeatedly held that it is not enough that the only embodiments, or all of the embodiments, contain a particular limitation to limit claims beyond their plain meaning.") (internal quotation marks omitted).

3. Administering terms

Claim Terms	Plaintiff's Proposal	Defendant's Proposal
"administered intravenously over 60 minutes infusion" ('299 Patent, claim 1; '594 Patent, claims 1, 28; '595 Patent, claims 1, 28; '596 Patent, claims 1, 28; '714 Patent, claim 1; '092 Patent, claim 1)	No construction is needed.	The claimed method requires that each intravenous infusion last 60 minutes.
"about 10 mg/kg of an anti-PDL1 antibody once every 2 weeks" ('299 Patent, claim 1; '594 Patent, claim 28; '595 Patent, claim 28; '596 Patent, claim 28; '092 Patent, claim 1)	No construction is needed.	"about 10 mg/kg of an anti-PD-L1 antibody every fourteen days." The claimed method is not practiced until a second dose has been administered, and ceases to be practiced if a subject is not treated 2 weeks after the preceding dose.

The parties dispute two terms from the Cogswell patents relating to the administration of the anti-PD-L1 antibody. BMS contends that both terms do not require construction. AstraZeneca contends that the terms require construction because the parties dispute how much flexibility is encompassed by the claims and whether subsequent administrations that are not "once every 2 weeks" or "over 60 minutes" still practice the method.

There is no dispute that the plain and customary meaning of "every 2 weeks" and "60 minutes" is clear. These terms therefore require no further construction. *See*

Summit 6, LLC v. Samsung Elecs. Co., 802 F.3d 1283, 1291 (Fed. Cir. 2015) ("Because the plain and ordinary meaning of the disputed claim language is clear, the district court did not err by declining to construe the claim term."). The disputes identified by AstraZeneca would not be resolved by its proposed constructions that swap "two weeks" for "fourteen days" and "administered . . . over 60 minutes" to "infusion last[ing] 60 minutes." *See EmeraChem Holdings, LLC v. Volkswagen Grp. of Am., Inc.*, 714 F. App'x 995, 997 (Fed. Cir. 2017) ("Claim construction is not an obligatory exercise in redundancy.") (internal quotation marks omitted).

The Court agrees with BMS that ruling on the issues AstraZeneca raises would be premature. Whether particular dosage regimens practice the claim is an issue of infringement, not claim construction. At the claim construction hearing, the parties discussed several hypotheticals regarding what exceptions could be made for patients unavailable to receive a subsequent dose precisely fourteen days after the preceding dose. This presents "a factual question of infringement" that is inappropriate to resolve as a part of claim construction. *Biotec Biologische Naturverpackungen GmbH & Co. KG v. Biocorp, Inc.*, 249 F.3d 1341, 1349 (Fed. Cir. 2001) (holding that no construction was necessary for the term "melting" where "the meaning of 'melting' d[id] not . . . depart from its ordinary meaning," and instead the parties disputed "the application of the melting step in the accused process"); *see also Acumed*, 483 F.3d at 806 ("After the court has defined the claim with whatever specificity and precision is warranted by the language of the claim and the evidence bearing on the proper construction, the task of determining whether the construed claim reads on the accused product is for the finder of fact.") (alterations accepted) (internal quotation marks omitted).

Similarly, whether a dosage regimen with subsequent administration steps still practices the claimed method is an infringement issue. *See VirnetX*, 792 F. App'x at 806 ("[A]s a general matter, an additional step does not defeat an infringement finding for a 'comprising' claim because infringement arises when all of the steps of a claimed method are performed, whether or not the infringer also performs additional steps.") (alterations accepted) (internal quotation marks omitted). The Court declines to address this infringement question at claim construction. *See Eon Corp. IP Holdings v. Silver Spring Networks*, 815 F.3d 1314, 1319 (Fed. Cir. 2016) ("[C]ourts should not resolve questions that do not go to claim scope, but instead go to infringement . . . .").

Conclusion

The disputed claim terms are construed in accordance with the conclusions set forth in this Memorandum Opinion and Order. The parties are directed to file a joint status report regarding the progress of discovery and any settlement discussions on May 31, 2023.

MATTHEW F. KENNELLY
United States District Judge

Date: April 21, 2023